

European patent office

11 Release number 0 025 859
A2

12 EUROPEAN PATENT REGISTRATION

21 Registration number: 80104830.7
22 Registration date: 14.08.8051 Int.Cl.³: C 07 D 249 / 08

30 Priority: 31.08.79 DE 2935164

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D - 6700 Ludwigshafen (DE)43 Release date of the registration:
01.04.81 patent paper 81 / 1372 Originator: Jacobs, Peter, Dr.
Kalmitstrasse 2
D - 6718 Gruenstadt (DE)84 Appointed contractual states:
AT BE CH DE FR GB IT LI LU NL SE72 Originator: Mangold, Dietrich, Dr.
Hermann - Walker - Strasse 49
D - 6903 Neckargemuend (DE)72 Originator: Oeser, Heinz - GUenter, Dr.
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54 procedure for manufacture of 1, 2, 4 - triazoles

57 Manufacture of 1, 2, 4 - triazole by conversion of 3 - amino - 1, 2, 4 - triazole with alcohol and nitrosation methods in the presence of water and sulphuric acid. The producible new compounds are valuable chemical reactants for the production of pharmaceutical products, chemical dyes and pest control methods.

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Procedure for production of 1, 2, 4 - triazoles

The invention refers to a new procedure of production of 1, 2, 4 - triazole by the conversion of 3 - amino - 1, 2, 4 - triazole with alcohol and nitrosation methods in the presence of water and sulphuric acids.

Pages 290 to 291 (1954) from J.Amer.Chem.Soc, Band 76 notifies, that one can get Tetrazol only with its tetrazoldiazoniumsalz , if one implements the diazotization from 5 - aminotetrazol in the presence of chemical hypophosphoric acids. It is specifically warned against the danger of the extremely explosive Diazoniumsalz and a safe process is seen only with the application of this acid. The same process is recommended due to the same

reason for the production of 1, 2, 4 – triazole by the deamination of 3 - amino - 1, 2, 4 – triazole and a profit of 75.3 percent is received. An assignment in Annalen, Band 273 (1893), page 144 points out in this context, that aminotetrazol explodes on its own in aqueous solution than Diazo - compound by 0° C.

Page 332 of the chemistry newspaper, Band 9 (1969) notifies, that one heats the hydrazinhydrat and 85 percent of owned formic acids to 200° C, the mixture comes to a freezing point by cooling and is replaced with sodium nitrite in aqueous, hydrochloric solution. One gets a profit of 55 – 60 % on an industrial scale 1, 2, 4 – triazole.

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Similarly (J.Chem.Soc., Band 109 (1916), pages 155 to 160) notifies that 5 - Amino - 1, 2, 4 – triazole, hydrochloric acids and sodium nitride or ethyl nitride are not replaced to 1, 2, 4 – triazole but to 5 - Chlor - 1, 2, 4 – triazole. One implements the replacement with saltpeter acids and the alkaline β - naphthol solution is set, one gets 1, 2, 4 – triazole - 5 - azo - β - naphthol. Similarly the production of 3 - methyl - 1, 2, 4 – triazole - 5 - azo - β - naphthol and 1, 2, 4 – triazole – 5 - azo - β - naphthylamine takes place with naphthylamine as Azo - components. One replaces 5 - amino - 3 - methyl - 1, 2, 4 - triazole with ethyl nitride and alcoholic hydrochloric acids, one receives 5 - chlor - 3 - methyl - 1, 2, 4 – triazole. The authors of the project points out the instability of the Diazo compounds of Amino - triazole under formation of Chlortriazole. One rechrystallizes 3 - Methyl - 1, 2, 4 – triazole - 5 - isodiazo hydroxide from ethyl alcohol, thus according to the author's opinion, one molecule of alcohol is added to this compound, which transforms itself in a normal Diazoniumsalz according to the author's opinion in a cool, concentrated sulphuric acids solution. Hence it should be pointed out that a formed diazoniumsalz is coupled for 3 - methyl - 1, 2, 4 – triazol - 5 - azo - β - naphthol in a sulphuric acid medium with alcoholic naphthol solution.

It was found that one gets favorable in non substituted 1, 2 and 4 - positions, in 2 - and / or 5 - position likewise by an aliphatic or aromatic residue substituted 1, 2, 4 - triazole by deamination of aminotriazole as per the use of nitrosation methods and acids in each case, if one converts in the 3 and / or 5 position by substituted aliphatic or aromatic residue of amino - 1, 2, 4 – triazole with aliphatic alcohol and nitrosation methods in the presence of water and sulphuric acids in each case.

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The conversion can be displayed in case of use of 3 - amino - 1, 2, 4 - triazol, sodium nitrite, sulphuric acids and alcohol by the following formulas: (diagram)

With regard to the status of the technology, the procedure delivers the patent in an easy and economic method 1, 2, 4 – triazole with better profit and purity, immediately on an industrial scale. The application of the severely approachable chemical hypophosphoric acids and an environmental pollution is thus avoided with phosphates. The procedure is

reliable than chemical reactants of applied process with regards to the all Diazo compounds, especially its transfer on a large scale, since no inclination of the reaction mixture should be observed for explosive corrosions. The formation on a large scale is avoided possibly on a safety critical diazonium - 1, 2, 4 - triazole. All these advantages according to the patents, immediately without use of chemical hypophosphoric acids, are surprising with respect to the status of the technology. Especially one could have expected the production of heterogeneous mixtures for the corrosive products, diazonium compounds, azo compounds, sulfo triazole or other nitric compounds.

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With the process - related patent, 1, 2, 4 - triazole of the formula are produced where the individual residuals R^1 can be same or different and a hydrogen atom or an aliphatic or an aromatic residue is signified in every case; they are producible with the 2, 1, 4 - triazole of the formula (diag) and 4, 2, 1 - triazole of the formula (diag) where the meaning mentioned before possesses tautomer and thus the end substances Ia and Ib by the process related patents.

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3 - amino - 1, 2, 4 - triazole of the formula (diag) and 5 - amino - 1, 2, 4 - triazole of the formula (diag) comes off as chemical reactants, which are considered tautomer together and are corresponding to the 3 - amino - 2, 1, 4 - triazole and 5 - amino - 2, 1, 4 - triazole of the formula (diag) and to the corresponding 3 - amino - 4, 2, 1 - triazole and 5 - amino - 4, 2, 1 - triazole of the formula (diag) wherein the individual residual R^1 can be same or different and signifies a hydrogen atom or an aliphatic or aromatic residue in each case.

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Furthermore 1 - amino - 1, 2, 4 - triazole of the formula (diag) comes off as chemical reactants, 2 - amino - 2, 1, 4 - triazole of the formula (diag) and 4 - amino - 4, 2, 1 triazole of the formula (diag) and thus general N - amino - 1, 2, 4 - triazole of the formula (diag) wherein the individual R^1 can be same or different and a hydrogen atom or an aliphatic or aromatic residual is signified for each case.

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Z signifies a sedentary amino group of a nitric atom, which means a single bond in each case for both the situated bonds a in α - position for amino group, which means a double bond in each case for both situated bonds a in α - position for amino group and the remaining bond a is identified in γ - position for amino groups, should be considered.

Preferred chemical reactants II and III and accordingly the preferred final reactants I are such that the formulae of the single residue R^1 can be same or different and signifies hydrogen atom, alkyl with 1 to 10 carbon atoms, especially an alkyl with 1 to 4 carbon atoms or phenyl. The residual R^1 mentioned before can be substituted by inert groups

under the reaction conditions, e.g. alkyl groups or alkoxyl groups with 1 to 3 carbon atoms in each case. E.g. following chemical reactants II and III are suitable: 1 - amino, 2 - amino, 3 - amino, 4 - amino, 5 - amino - 1,2, 4 - triazole; homologous in 3 - position or once in 5 - position, or twice in 3 - position or 5 - position, same or different by the Methyl - ethyl - , propyl - , isopropyl - , butyl - , isobutyl - , sec. - butyl - , phenyl - , tert. - butyl - group of substituted aminotriazole.

Chemical reactants II and III are converted in stoichiometric quantity or with an excess of alcohol, preferably in quantity of 3 to 30, especially by 5 to 15 equivalents (Mol divided by the number of hydroxyl groups in molecule) alcohol for every Mol of chemical reactants II or III. Alcohols can be aliphatic mono - or poly alcohols. Preferred alcohols are the formula (diagram), wherein R^3 means an alkyl with 1 to 5 carbon atoms or the residual $HO - R^4$, in which R^4 is an aliphatic residual, especially an alkyl with 2 to 4 carbon atoms.

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The residual $R^5O - (R^4O)_n - R^4$, means the single residual R^4 can be same or different and stands for an aliphatic residual, especially an alkyl with 2 to 4 carbon atoms, especially signifies an alkyl with 1 to 4 carbon atoms and n stands for the numbers 4, 3, 2 or in particular 1. The residuals R^3 , R^4 , and R^5 can be substituted by inert groups e.g. alkyl groups or alkoxy groups under reaction conditions with 1 or 3 carbon atoms in each case.

Alcohol V should be considered as e.g. methanol, alcohol, n - and i - propanol, n - butanol, butanol - 2, isobutanol, ethylenglykol, diaethylenglikol, methylethylenglykol, n - pentanol, neopentylglykol, 1, 3 - propylenglykol, 1, 4 - gutandiol, 1, 2 - propylenglykol, triethylenglykol, diethylenglykol - mono - n - butylaether; or a corresponding mixture. Alcohol, isopropanol, methylethylenglykol, n - propanol, isobutanol are preferred.

Furthermore one uses nitrosation methods during reaction, e.g. nitrous acids and reactants, which is converted in nitrous acids under reaction conditions, like nitrous gases; salts, preferred alkali salts, nitrous acids, especially potassium nitrate; ester of nitrous acids, appropriate alkyl nitrite. An addition of alcohol can be completely or partially done without during the use of alkyl nitrite, since such nitrite can appropriately replace a combination of nitrous acids and alcohol under the reaction conditions.

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In such cases, a ratio of 1 to 5 equivalents of alcohol for every Mol chemical reactants II or III are appropriate. Preferably in case of esters, alkyl nitrite with 1 to 6 carbon atoms, e.g. ethyl - , n - propyl, n - isopropyl - nitrite, n - butyl, isobutyl, sec. - butyl, tert. butyl, amyl - , isoamyl - nitrite and in particular methyl nitrite should be considered. Under nitrous gases, the known nitric tetroxides nitric monoxide, nitric dioxide, nitric tetroxide, dinitric trioxide are understood here as nitrosation methods. They can be used individually or appropriately in an appropriate mixture, favorably by nitric monoxide and

nitric dioxide. In general, quantities of 1.1 to 5 Mol alkyl nitrite, nitrous acids ester and / or nitrous gases for every Mol of chemical reactants II or III, 1.1 to 2.7, in particular 1.1 to 1.7 Mol of alkyl nitrite and / or nitrous acids ester or 1.5 to 5, in particular 2 to 4 Mol N^2O^3 for each Mol of chemical reactants II or II should be considered. The mentioned nitric oxides and / or gas mixtures can be added to inert gases, e.g. nitrogen under the reaction conditions.

Similarly glycol of nitrous acids should be used as nitrosation methods. These ester of nitrous acids can be produced optionally, appropriately as per described procedure in the German publication script 21 44 420, by the conversion of glycol or glycol derivatives with nitrous acids or nitric acids. Preferred ester of glycols and glycol derivatives are mono - or diglycol of nitrous acids of the formula (diag) wherein the residue $R^7 - O -$ or the residue $(CH_{R2} - CH_2O)^n$ means R^7 signifies an aliphatic residual and R^2 signifies hydrogen atom or an aliphatic residual, n stands for the number 1, 2, 3 or 4 and X signifies the group - NO or an aliphatic residual.

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Favorably R^7 signifies an alkyl residual with 3 to 12, especially 4 to 9 carbon atoms, R^2 signifies hydrogen atom or an alkyl residual with 1 to 4 carbon atoms, in particular the methyl groups, n stands for the number 1, 2 or 3 and X means the group -NO or an alkyl residual with 1 to 4 carbon atoms. The mentioned alkyl residuals and alkaline residuals can be geradkettig or derived. Favorable residuals which are mentioned before can be substituted by inert groups e.g. alkoxy groups, alkyl groups with 1 to 3 carbon atoms for each case under reaction conditions. In general quantities from 1.1 to 5 Mol of monoglycol for every Mol of chemical reactants II or III, 1.1 to 2.7, in particular 1.1 to 2.2 Mol monoglycol for every Mol of chemical reactant II or III should be considered. One accordingly selects quantities of 0.55 to 1.1 Mol of Diglycol for every Mol of chemical reactants II or III. Suitable esters IV are for example mono - and / or diester of nitrous acids with the following compounds:

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Diglycolester, where R^6 means the residual $R^7 - O$, X means the group -NO and R & means the alkyl residue $(CH_2) - 3 - (CH_2) 4$

The conversion is executed under the addition of water, favorably in a quantity of 5 to 100, especially from 15 to 50 Mol of water for every chemical reactant II or III; water can be separated and / or e.g. added by aqueous acids, by aqueous alkali nitrite solutions or by mixtures of alcohol with water. The water formed on its own during reaction is not defined in this connection as added water and is not contained in the preferable water quantity mentioned above.

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The conversion is executed in the presence of nitrous acids, favorably in a quantity of 1.5 to 15, in particular from 2.5 to 10 equivalent acids referring to chemical reactants II or III. The acids can be used in a concentrated form or with a solution, in particular water.

The conversion is continuously or intermittently executed with a temperature of at least - 20 ° C, in the rule with a temperature of - 5 ° C up to a boiling temperature of the mixture, appropriately from 0 to 200 ° C, preferably from 0 to 50 ° C, depressurized or under pressure. In the rule, components of the chemical batch, e.g. water, alcohol or acids, or the total chemical batch serve as a solution of the reaction.

The reaction can be executed as follows: a mixture of chemical reactants II or III, alcohol, nitrosation methods, acids, and water is retained for 1.5 to 5 hours of the reaction temperature. Appropriately one may taper off the nitrosation methods, e.g. the aqueous sodium nitrite solution, or the nitrous acids ester for the mixture of the reaction partner. The supply can take place fast in any large area. End of the reaction coincides frequently with the end of the supply of the nitrosation methods. End substances are cut off due to the reaction mixture in a standard way, e.g. by an alkaline adjustment of the mixture, filtration, restriction of filtrates, extraction with a suitable solvent like methanol or dioxine, filtration and distillation of filtrates.

According to the procedure of the patent, the producible new compounds are valuable chemical reactants for the production of pharmaceutical products, chemical dyes and pest control methods. With reference to the usage, the releases mentioned before and DE - AS 17 95 249, DE - OS 27 20 949, DE - OS 24 01 715, DE - OS 24 31 407, DE - OS 27 13 777, DE - OS 24 06 665 are referenced.

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The mentioned part means part by weight in the examples.

Example 1

One enters 84 parts 3 - amino - 1, 2, 4 - triazole in 360 parts isopropanol and 200 parts of water and then shifts the mixture with 210 parts of concentrated sulphuric acids (98 percent by weight). One agrees to a solution of 133 parts of sodium nitrite in 300 parts of water within 30 minutes at 5 ° C, whereby nitrogen is formed. One melts the mixture for 3 hours at room temperature; pH - value of 7.8 is adjusted during this temperature with 50 - percent by weight of sodium hydroxide solution, cools the mixture at 10 ° C and exhausts the unusual sodium sulphate. The filtrate is concentrated in the vacuum for dry friction and decocted twice with every 500 parts of methanol. The filtrate from the solvent is released in the vacuum after filtration. One gets 65.6 parts of 1, 2, 4 - triazole (95 % of the theory profit) from the melting point 117 ° C.

Example 2

One enters 84 parts of 4 - amino - 1, 2, 4 - triazole in a mixture of 360 parts of isopropanol and 400 parts of water and then shifts the mixture with 210 parts of concentrated sulphuric acids (98 percent by weight). One agrees to a solution of 133 parts of sodium nitrite in 300 parts of water within 30 minutes at 5 ° C, whereby nitrogen is formed. One melts the mixture for 3 hours at room temperature; pH - value of 7.8 is adjusted during this temperature with 50 - percent by weight of sodium hydroxide solution, cools the mixture at 10 ° C and exhausts the unusual sodium sulphate.

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The filtrate is concentrated in the vacuum for dry friction and decocted twice with every 500 parts of methanol. The filtrate from the solvent is released in the vacuum after filtration. One gets 64.9 parts of 1, 2, 4 - triazole (94 % of the theory profit) from the melting point 117 ° C.

Example 3

One adds 84 parts of 3 - amino - 1, 2, 4 - triazole in a mixture of 400 parts of ethyl and 500 parts of water and then shifts the mixture with 210 parts of concentrated sulphuric acids (98 percent by weight). One agrees to a solution of 133 parts of sodium nitrite in 300 parts of water within 30 minutes at 5 ° C, whereby nitrogen is formed. One melts the mixture for 3 hours at room temperature; pH - value of 7.8 is adjusted during this temperature with 50 - percent by weight of sodium hydroxide solution, cools the mixture at 10 ° C and exhausts the unusual sodium sulphate. The filtrate is concentrated in the vacuum for dry friction and decocted twice with every 500 parts of methanol. The filtrate is concentrated in the vacuum for dry friction after washing with 100 parts of alcohol and the received residue is decocted twice with every 500 parts of dioxine. The filtrate from the solvent is released in the vacuum after filtration. One gets 60.7 parts of 1, 2, 4 - triazole (88 % of the theory profit) from the melting point 117 ° C.

Example 4

One adds 49 parts of 3 - amino - 5 - methyl - 1, 2, 4 - triazole in a mixture of 400 parts of isopropanol and 500 parts of water and finally shifts the mixture with 105 parts of concentrated sulphuric acids (98 percent by weight). One agrees to a solution of 67 parts of sodium nitrite in 150 parts of water within 30 minutes at 5 ° C, whereby nitrogen is formed.

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One melts the mixture for 3 hours at room temperature; pH - value of 7.8 is adjusted during this temperature with 50 - percent by weight of sodium hydroxide solution, cools the mixture at 0 ° C and exhausts the unusual sodium sulphate. The filtrate is released from the solvent in the vacuum after washing with 100 parts and the received residue is decocted twice with every 300 parts of dioxine. The combined dioxine solutions are

concentrated for dry friction in vacuum. One gets 29 parts of 3 - methyl - 1, 2, 4 - triazole (94 % of the theory profit) from the melting point 117 ° C.

Example 5

One adds 160 parts of 3 - amino - 5 - phenyl - 1, 2, 4 - triazole in a mixture of 400 parts of isopropanol and 500 parts of water and then shifts the mixture with 210 parts of concentrated sulphuric acids (98 percent by weight). One agrees to a solution of 133 parts of sodium nitrite in 300 parts of water within 30 minutes at 5 ° C, whereby nitrogen is formed. One melts the mixture for 3 hours at room temperature; pH - value of 7.8 is adjusted during this temperature with 50 - percent by weight of sodium hydroxide solution, cools the mixture at 5 ° C and exhausts the unusual sodium sulphate. The filtrate is released from the solvent in the vacuum after washing with 150 parts of isopropanol and the received residue is decocted once with every 500 parts of dioxine. One gets 100 parts of 3 - phenyl - 1, 2, 4 - triazole (69 % of the theory profit) from the melting point 117 ° C after the separation of the dioxine.

Example 6

One enters 84 parts of 3 - amino - 1, 2, 4 - triazole in a mixture of 500 parts of glycol monoethylaether and then shifts the mixture with 800 parts of 50 - percent by weight sulphuric acid at 25 ° C.

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One agrees to a solution of 90 parts of sodium nitrite in 150 parts of water within 30 minutes at 5 ° C. One melts the mixture for 3 hours at 25 ° C; pH - value of 7.8 is adjusted during this temperature with 50 - percent by weight of sodium hydroxide solution, cools at 10 ° C and exhausts the failed sodium sulphate. The filtrate is released from the solvent in the vacuum and residue is decocted twice with every 300 parts of dioxine. The combined dioxine solution is concentrated in vacuum for dry friction. The end substances are washed and dried with aether. One gets 49 parts of 1, 2, and 4 - triazole (71 % of the theory profit) from the melting point 116 ° C.

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Patent claims

Procedure for production in 1, 2, and 4 - position which is not substituted, in 3 - and / or 5 - position similarly by an aliphatic or aromatic residue of substituted 1, 2, 4 triazole by deamination of aminotriazole under the use of nitrosation methods and acids, thus indicates, that one converts in 3 and / or 5 position by an aliphatic or aromatic residue of substituted amino - 1, 2, 4 triazole with aliphatic alcohols and nitrosation methods in the presence of water and sulphuric acids.

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